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| Term | Documents |
|--|-----------|
| HYALURONIC | 9420 |
| HYALURONICS | 1 |
| ACID | 1796321 |
| ACIDS | 558322 |
| (2 AND (HYALURONIC ADJ ACID)).USPT,PGPB,JPAB,EPAB,DWPI. | 7 |
| (L2 AND HYALURONIC ACID).USPT,PGPB,JPAB,EPAB,DWPI. | 7 |

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IBM Technical Disclosure Bulletins

Search:

L5

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|--|--------------------------|------------------|-----------------|
| side by side | | | result set |
| <i>DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ</i> | | | |
| <u>L5</u> | l2 and hyaluronic acid | 7 | <u>L5</u> |
| <i>DB=USPT,PGPB; PLUR=YES; OP=ADJ</i> | | | |
| <u>L4</u> | hyaluronic acid | 6669 | <u>L4</u> |
| <u>L3</u> | L2 and hyalur\$ | 18 | <u>L3</u> |
| <u>L2</u> | L1 and metastasis | 291 | <u>L2</u> |
| <u>L1</u> | multidrug adj resistance | 1395 | <u>L1</u> |

END OF SEARCH HISTORY

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS

RN 9004-61-9 REGISTRY

CN Hyaluronic acid (8CI, 9CI) (CA INDEX NAME)

OTHER NAMES:

CN ACP

CN ACP (polysaccharide)

CN ACP gel

CN Durolane

CN HA 9

CN **Hyaluronan**

CN Hylan G-F 20

CN Hylartil

CN Luronit

CN Mucoitin

CN Sepracoat

CN Sofast

CN Synvisc

DR 9039-38-7, 37243-73-5, 29382-75-0

MF Unspecified

CI PMS, COM, MAN

PCT Manual registration, Polyester, Polyester formed

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS,
BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN,
CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGU,
DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*,
NAPRALERT, NIOSHTIC, PHAR, PHARMASEARCH, PIRA, PROMT, TOXCENTER, USAN,
USPAT2, USPATFULL

(*File contains numerically searchable property data)

Other Sources: DSL**, EINECS**, TSCA**

(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

10152 REFERENCES IN FILE CA (1957 TO DATE)

741 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

10167 REFERENCES IN FILE CAPLUS (1957 TO DATE)

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L5: Entry 6 of 7

File: USPT

Oct 6, 1998

DOCUMENT-IDENTIFIER: US 5817321 A

**** See image for Certificate of Correction ****

TITLE: Biological agent compositions

Brief Summary Text (19):

In another embodiment, the invention provides a method of preventing or limiting tumor metastases by administering one of the anticancer compositions of the invention.

Drawing Description Text (13):

FIG. 9 shows the inhibition of tumor metastasis in mice treated with doxorubicin with Pluronic P85 vs. mice treated with doxorubicin alone.

Detailed Description Text (4):

It has been discovered that the effectiveness of the block copolymers of the invention in enhancing the potency of chemotherapeutic drugs and reversing MDR is highly dependent (a) on the hydrophobe percentage and (b) on the hydrophobe weight. The effectiveness increases with either an increase in the percentage (a) or an increase in weight (b), or both. These hydrophobe percentage and hydrophobe weight increases also correlate with improved micelle formation properties wherein micelle formation for these copolymers occurs at lower concentrations. See, Hurter et al., *Macromolecules* 26: 5030, 1993; Hurter et al., *Macromolecules* 26: 5592, 1993; Alexandris et al., *Macromolecules* 27: 2414, 1994. While not wishing to be limited to a particular theory, it is believed that micelle formation serves as a surrogate for measuring the physical properties that lead to improved biological agent delivery properties. Again, not wishing to be limited to a particular theory, it is believed that it is not micelles per se that lead to improved biological agent efficiency and reversion of multidrug resistance. If, using doxorubicin as a model biological agent, the ratio of (a) the IC_{sub.50} (a measure of effective cytotoxicity concentration) for a copolymer-containing composition to (b) the IC_{sub.50} for free doxorubicin is plotted against the concentration of copolymer, the plot is biphasic, with a rapid decrease in the ratio seen as copolymer concentrations increase but remain under the CMC of the copolymer. Above the CMC, a rapid leveling off of the ratio is observed. See FIG. 6B. Maximal enhancement of biological agent activity occurs above the CMC, although enhancement activity is seen at concentrations, for the copolymer Pluronic L61, as low as 0.0001% wt/vol, or less. The micellar form is also believed to be important to using the copolymers in drug delivery for other reasons, as will be discussed below.

Detailed Description Text (10):

Members of the glycoprotein P family of membrane proteins are believed to be responsible for the multidrug resistance of many of the tumors whose resistance can be reversed using the compositions of the invention. See, Goldstein et al., *Cancer Treatment Res.* 57: 101-119, 1991. These proteins are believed to function as pumps that export the biological agent against which the tumors have become resistant. Members of the same protein family are believed to reside in the membranes of the endothelial cells lining blood vessels in the brain and to be responsible for the "blood-brain barrier" (BBB) that excludes effective amounts of many biological agents from the entering the brain. See, for example, Tatsuta et al., *J. Biol. Chem.* 267: 20383-20391. Compositions of the present invention can be used to enhance drug permeability into the brain, as discussed in more detail in U.S. application Ser. No. 08/478,979, filed concurrently herewith on Jun. 7, 1995 and entitled

"Compositions for Targeting Biological Agents," the entire disclosure of which is incorporated herein by reference. Further, members of this protein family are believed to be responsible for drug resistance in certain Candida, malaria and other microbial infections. Without wishing to be bound to a particular theory, it is believed that the compositions of the invention reverse efflux mechanisms mediated by members of the glycoprotein P family and other drug resistance mechanisms.

Detailed Description Text (42):

The pharmaceutical compositions of the invention can be administered by a number of routes, including without limitation orally, topically, rectally, vaginally, by pulmonary route, for instance, by use of an aerosol, or parenterally, including but not limited to intramuscularly, subcutaneously, intraperitoneally or intravenously. The compositions can be administered alone, or can be combined with a pharmaceutically-acceptable carrier or excipient according to standard pharmaceutical practice. For the oral mode of administration, the compositions can be used in the form of tablets, capsules, lozenges, troches, powders, syrups, elixirs, aqueous solutions and suspensions, and the like. In the case of tablets, carriers that can be used include lactose, sodium citrate and salts of phosphoric acid. Various disintegrants such as starch, and lubricating agents such as magnesium stearate, sodium lauryl sulfate and talc, are commonly used in tablets. For oral administration in capsule form, useful diluents are lactose and high molecular weight polyethylene glycols. When aqueous suspensions are required for oral use, the compositions can be combined with emulsifying and suspending agents. If desired, certain sweetening and/or flavoring agents can be added. For parenteral administration, sterile solutions of the conjugate are usually prepared, and the pHs of the solutions are suitably adjusted and buffered. For intravenous use, the total concentration of solutes should be controlled to render the preparation isotonic. For ocular administration, ointments or droppable liquids may be delivered by ocular delivery systems known to the art such as applicators or eye droppers. Such compositions can include mucomimetics such as hyaluronic acid, chondroitin sulfate, hydroxypropyl methylcellulose or poly(vinyl alcohol), preservatives such as sorbic acid, EDTA or benzylchromium chloride, and the usual quantities of diluents and/or carriers. For pulmonary administration, diluents and/or carriers will be selected to be appropriate to allow the formation of an aerosol.

Detailed Description Text (48):

Generally, the biological agents used in the invention are administered to an animal in an effective amount. The effect of the copolymer used in the composition on effectiveness must be considered in determining effective amount. Generally, an effective amount is an amount effective to either (1) reduce the symptoms of the disease sought to be treated or (2) induce a pharmacological change relevant to treating the disease sought to be treated. For cancer, an effective amount includes an amount effective to: reduce the size of a tumor; slow the growth of a tumor; prevent or inhibit the formation of metastases; or increase the life expectancy of the affected animal.

WEST**End of Result Set**☐ **Generate Collection** **Print**

L5: Entry 7 of 7

File: USPT

Mar 12, 1996

DOCUMENT-IDENTIFIER: US 5498613 A

TITLE: Dipyridamole and analogs thereof in preventing adhesion formation

Brief Summary Text (17):

Clinically, dipyridamole has been used primarily to reduce postoperative thromboembolism, particularly in patients with heart valve replacements and artificial heart valves [Mammen, E. F., "An overview of dipyridamole," Thrombosis Research Supplement XII, 1 (1990)]. It is believed that this occurs through inhibition of platelet aggregation mediated by adenosine [Boeynaems, J. M. et al., "Dipyridamole and vascular prostacyclin production," Biochemical Pharmacol. 35, 2897 (1986); Tzanakakis, G. N. et al., "Prevention of human pancreatic cancer cell-induced hepatic metastasis in nude mice by dipyridamole and its analog RA-233," Cancer 71, 2466 (1993)] and/or through an increase in PGI.sub.2 production [Constantini, V. et al., "Increased prostacyclin production from human veins by dipyridamole: an in vitro and ex vivo study," Biomed. Biochim. Acta 49, 263 (1990)]. In addition, dipyridamole has been shown to have utility as a vasodilator, particularly in diagnostic assays [Stringer, K. A. et al., "Disposition of oral dipyridamole in patients undergoing thallium 201 myocardial imaging," Pharmacotherapy 12, 83 (1992)] and as an adjunct to other chemotherapeutic agents, making it possible to kill tumor cells at a lower concentration of antineoplastic drug [see, e.g., Czejka, M. J. et al., "Clinical pharmacokinetics of 5-fluorouracil," Drug Res. 43, 387 (1993); Isonishi, S., "Phase I and Pharmacokinetic Trial of Intraperitoneal Etoposide in Combination with the Multidrug-Resistance -Modulating Agent Dipyridamole," J. Nat'l Cancer Inst. 83, 621 (1991)].

Brief Summary Text (35):

Yet another suitable approach for single dose delivery of active agent in accordance with the present invention involves the use of so-called viscous instillates. In this technique, high-molecular-weight carriers are used in admixture with the active agents, giving rise to an extended structure which produces a solution with high viscosity. Suitable high-molecular-weight carriers include, but are not limited to, the following: dextrans and cyclodextrans; hydrogels; crosslinked viscous materials, including viscoelastics and cross-linked viscoelastics; carboxymethylcellulose; and hyaluronic acid. While some studies have suggested that the use of viscous barrier solutions per se may have an advantageous effect in reducing the incidence of adhesion formation, it is believed that any such effect is of limited scope when compared to the combination of active agent and carrier. The intraperitoneal administration of a viscous instillate comprising tolmetin is described in Abe, H. et al., "The Effect of Intraperitoneal Administration of Sodium Tolmetin -Hyaluronic Acid on the Postsurgical Cell Infiltration In Vivo," J. Surg. Res. 49:322 (1990), the entire disclosure of which is hereby incorporated by reference.

Other Reference Publication (36):

Isonishi et al., "Phase I and Pharmacokinetic Trial of Intraperitoneal Etoposide in Combination With the Multidrug-Resistance -Modulating Agent Dipyridamole", Journal of the National Cancer Institute, vol. 83, Issue 9, pp. 621-626 (May 1, 1991).

Other Reference Publication (45):

Tzanakakis et al., "Prevention of Human Pancreatic Cancer Cell-Induced Hepatic Metastasis in Nude Mice by Dipyridamole and Its Analog RA-233", Cancer, vol. 71,

Issue 8, pp. 2466-2471 (Apr. 15, 1993).

CLAIMS:

13. A method according to claim 12, wherein the instillate comprises a high-molecular-weight carrier selected from the group consisting of dextrans, cyclodextrans, hydrogels, carboxymethylcellulose, hyaluronic acid, chondroitin sulfate and mixtures thereof.

WEST

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L5: Entry 5 of 7

File: USPT

Nov 24, 1998

DOCUMENT-IDENTIFIER: US 5840319 A
TITLE: Biological agent compositions

Brief Summary Text (19):

In another embodiment, the invention provides a method of preventing or limiting tumor metastases by administering one of the anticancer compositions of the invention.

Drawing Description Text (13):

FIG. 9 shows the inhibition of tumor metastasis in mice treated with doxorubicin with Pluronic P85 vs. mice treated with doxorubicin alone.

Detailed Description Text (4):

It has been discovered that the effectiveness of the block copolymers of the invention in enhancing the potency of chemotherapeutic drugs and reversing MDR is highly dependent (a) on the hydrophobe percentage and (b) on the hydrophobe weight. The effectiveness increases with either an increase in the percentage (a) or an increase in weight (b), or both. These hydrophobe percentage and hydrophobe weight increases also correlate with improved micelle formation properties wherein micelle formation for these copolymers occurs at lower concentrations. See, Hurter et al., *Macromolecules* 26: 5030, 1993; Hurter et al., *Macromolecules* 26: 5592, 1993; Alexandris et al., *Macromolecules* 27: 2414, 1994. While not wishing to be limited to a particular theory, it is believed that micelle formation serves as a surrogate for measuring the physical properties that lead to improved biological agent delivery properties. Again, not wishing to be limited to a particular theory, it is believed that it is not micelles per se that lead to improved biological agent efficiency and reversion of multidrug resistance. If, using doxorubicin as a model biological agent, the ratio of (a) the IC₅₀ (a measure of effective cytotoxicity concentration) for a copolymer-containing composition to (b) the IC₅₀ for free doxorubicin is plotted against the concentration of copolymer, the plot is biphasic, with a rapid decrease in the ratio seen as copolymer concentrations increase but remain under the CMC of the copolymer. Above the CMC, a rapid leveling off of the ratio is observed. See FIG. 6B. Maximal enhancement of biological agent activity occurs above the CMC, although enhancement activity is seen at concentrations, for the copolymer Pluronic L61, as low as 0.0001% wt/vol, or less. The micellar form is also believed to be important to using the copolymers in drug delivery for other reasons, as will be discussed below.

Detailed Description Text (10):

Members of the glycoprotein P family of membrane proteins are believed to be responsible for the multidrug resistance of many of the tumors whose resistance can be reversed using the compositions of the invention. See, Goldstein et al., *Cancer Treatment Res.* 57: 101-119, 1991. These proteins are believed to function as pumps that export the biological agent against which the tumors have become resistant. Members of the same protein family are believed to reside in the membranes of the endothelial cells lining blood vessels in the brain and to be responsible for the "blood-brain barrier" (BBB) that excludes effective amounts of many biological agents from the entering the brain. See, for example, Tatsuta et al., *J. Biol. Chem.* 267: 20383-20391. Compositions of the present invention can be used to enhance drug permeability into the brain, as discussed in more detail in U.S. application Ser. No. 08/478,979, filed concurrently herewith on Jun. 7, 1995 and entitled "Compositions for Targeting Biological Agents," the entire disclosure of which is

incorporated herein by reference. Further, members of this protein family are believed to be responsible for drug resistance in certain Candida, malaria and other microbial infections. Without wishing to be bound to a particular theory, it is believed that the compositions of the invention reverse efflux mechanisms mediated by members of the glycoprotein P family and other drug resistance mechanisms.

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Detailed Description Text (49):

Generally, the biological agents used in the invention are administered to an animal in an effective amount. The effect of the copolymer used in the composition on effectiveness must be considered in determining effective amount. Generally, an effective amount is an amount effective to either (1) reduce the symptoms of the disease sought to be treated or (2) induce a pharmacological change relevant to treating the disease sought to be treated. For cancer, an effective amount includes an amount effective to: reduce the size of a tumor; slow the growth of a tumor; prevent or inhibit the formation of metastases; or increase the life expectancy of the affected animal.

CLAIMS:

13. A method of inhibiting or preventing tumor metastases comprising administering at tumor metastasis inhibiting or preventing amount of the composition of claim 1.

17. A composition to overcome multidrug resistance in cancer cells to cytotoxic drugs, comprising an effective amount of at least one cytotoxic drug from the group consisting of anthracycline and drugs related to multidrug resistance solubilized in non-toxic, pharmaceutically acceptable polymeric micelles.

18. A method to overcome multidrug resistance in cancer cells to cytotoxic drug in the treatment of cancer with the cytotoxic drugs, comprising administering to a patient in chemotherapy an effective amount of at least one cytotoxic drug solubilized in non-toxic, pharmaceutically acceptable polymeric micelles.

WEST**Number of documents to display is limited to 10 for FULL format****Generate Collection****Print****Search Results - Record(s) 1 through 2 of 2 returned.**☐ 1. Document ID: JP 61000017 A

L1: Entry 1 of 2

File: JPAB

Jan 6, 1986

PUB-NO: JP361000017A

DOCUMENT-IDENTIFIER: JP 61000017 A

TITLE: MUCOPOLYSACCHARIDE-TYPE CANCER-METASTATIS SUPPRESSING AGENT

PUBN-DATE: January 6, 1986

INVENTOR-INFORMATION:

NAME

COUNTRY

SAKURAI, KATSUKIYO

HORIE, KATSUYUKI

SAKAMOTO, TAKASHI

OKUYAMA, TAKASHI

ASSIGNEE-INFORMATION:

NAME

COUNTRY

SEIKAGAKU KOGYO CO LTD

APPL-NO: JP59118283

APPL-DATE: June 11, 1984

US-CL-CURRENT: 514/54

INT-CL (IPC): A61K 31/725; C08B 37/00

ABSTRACT:

PURPOSE: To provide the titled suppressing agent containing hyaluronic acid (HA) or crosslinked HA, absolutely free from side effects such as myelotic disorder, cardiotoxicity, alopecia, etc. and expected to have excellent effect to highly metastatic malignant tumor.

CONSTITUTION: HA obtained from funis, crest, vitreous body, etc. and having a molecular weight of several thousands \sim several millions (preferably having an intrinsic viscosity of 0.2 \sim 30, i.e. molecular weight of 4,000 \sim 2,000,000), or a crosslinked HA obtained by crosslinking HA or its salt with a polyfunctional epoxy compound and having a crosslinking number of \geq 5 per 1,000 recurring disaccharide units composed of glucuronic acid of HA and N-acetylglucosamine, or its salt, is used as an active component of the present agent. The suppressing agent actively synthesizes proteoglycan, and suppresses the metastasis of various malignant tumor existing at the surface of cells. It is expected to be effective against malignant melanoma, fibrosarcoma, etc.

COPYRIGHT: (C)1986, JPO&Japio

| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWC |
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|-----|
| Draw | Desc | Image | | | | | | | | | |

☐ 2. Document ID: JP 61000017 A JP 92056805 B

L1: Entry 2 of 2

File: DWPI

Jan 6, 1986

DERWENT-ACC-NO: 1986-045778
DERWENT-WEEK: 198607
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TITLE: Carcinoma metastasis-inhibiting muco-polysaccharide drug - contains
hyaluronic acid or crosslinked hyaluronic acid or their salt

PATENT-ASSIGNEE:

| | |
|------------------------|-------|
| ASSIGNEE | CODE |
| SEIKAGAKU KOGYO CO LTD | SE GK |

PRIORITY-DATA: 1984JP-0118283 (June 11, 1984)

PATENT-FAMILY:

| PUB-NO | PUB-DATE | LANGUAGE | PAGES | MAIN-IPC |
|---------------|-------------------|----------|-------|-------------|
| JP 61000017 A | January 6, 1986 | | 013 | |
| JP 92056805 B | September 9, 1992 | | 013 | A61K031/725 |

APPLICATION-DATA:

| PUB-NO | APPL-DATE | APPL-NO | DESCRIPTOR |
|--------------|---------------|----------------|------------|
| JP 61000017A | June 11, 1984 | 1984JP-0118283 | |
| JP 92056805B | June 11, 1984 | 1984JP-0118283 | |
| JP 92056805B | | JP 61000017 | Based on |

INT-CL (IPC): A61K 31/72; A61K 31/725; C08B 37/08

ABSTRACTED-PUB-NO: JP 61000017A

BASIC-ABSTRACT:

Carcinoma metastasis inhibiting mucopolysaccharide drug, which is hyaluronic acid (HA) or crosslinked HA or their salt, as active ingredient.

M.W. of HA used is several thousand-several million. Crosslinked HA is crosslinked by multifunctional epoxy cpd. to HA or its salt, while crosslinked number is more than 5 against 1000-repeated disaccharide of HA. As multifunctional epoxy cpd., halomethyloxirane cpd. or bisepoxy cpd. eq. epichlorohydrin is used. Crosslinked HA has resistance to hyaluronidase.

More than 1.0% of HA is dissolved in alkaline aq. soln. and pref. more than 50% of H₂O sol. org. solvent. eq. alcohol, acetone, dioxane, against total soln. is added. Pref. pH is 12-14. Then multifunctional epoxy cpd. is added and reacted at 10-60 deg.C, pref. at 20-40 deg.C for 24-2 hrs.. Crosslinking ratio of crosslinked HA or its salt is regulated by changing mol ratio of HA or its salt and multifunctional epoxy cpd.. Pref. HA used in this invention has intrinsic viscosity 0.2-30, m.w. 4000-2000000. This drug is used as several dosage forms. Clinical dose for adult is normally, as HA or crosslinked HA, 25mg-5 g/day (p.o.) and 10 mg-2.5 g/l dose (inj).

ADVANTAGE - Drug has no side effects as other anticancer drugs and has analgesic and tissue restoration effect.

CHOSEN-DRAWING: Dwg.0/0

TITLE-TERMS: CARCINOMA METASTASIS INHIBIT MUCO POLYSACCHARIDE DRUG CONTAIN
HYALURONIC ACID CROSSLINK HYALURONIC ACID SALT

DERWENT-CLASS: A96 B04

CPI-CODES: A03-A; A12-V01; B04-C02E; B12-D01; B12-G07; B12-J01;

CHEMICAL-CODES:

Chemical Indexing M1 *01*

Fragmentation Code

J0 J012 J1 J111 J3 J321 L814 L832 L834 M210
M211 M262 M280 M281 M320 M423 M781 M903 P411 P633
P714 V735

UNLINKED-DERWENT-REGISTRY-NUMBERS: 0272U; 1740U

POLYMER-MULTIPUNCH-CODES-AND-KEY-SERIALS:

Key Serials: 0211 0231 1282 1989 2001 2008 2020 2286 2299 2300 2318 2507 2509 2559 2578 2585
2606 2607 2672 2675 2766

Multipunch Codes: 014 04- 075 226 231 24- 244 259 311 316 332 341 398 42- 473 48- 512 525 541
544 545 57- 575 583 589 62- 645 722

SECONDARY-ACC-NO:

CPI Secondary Accession Numbers: C1986-019289

| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC |
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|------|
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jp-61000017\$.did.

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L27: Entry 162 of 162

File: DWPI

Nov 16, 1995

DERWENT-ACC-NO: 1996-010551
DERWENT-WEEK: 200131
COPYRIGHT 2003 DERWENT INFORMATION LTD

TITLE: Treatment of cancers and redn. of cancer metastases - by admin. of dosage
forms which contain e.g. sodium hyaluronate with a mol. wt. below 750000 Daltons

INVENTOR: ASCULAI, S S; FALK, R E

PATENT-ASSIGNEE:

| | |
|--------------------------|-------|
| ASSIGNEE | CODE |
| HYAL PHARM CORP | HYALN |
| NORPHARMCO INC | NORPN |
| HYALURONIC ACID DRUG INC | HYALN |

PRIORITY-DATA: 1994CA-2122519 (April 29, 1994)

PATENT-FAMILY:

| PUB-NO | PUB-DATE | LANGUAGE | PAGES | MAIN-IPC |
|---------------|--------------------|----------|-------|-------------|
| WO 9530423 A2 | November 16, 1995 | E | 271 | A61K031/725 |
| CN 1151118 A | June 4, 1997 | | 000 | A61K031/725 |
| AU 9524023 A | November 29, 1995 | | 000 | A61K031/725 |
| CA 2122519 A | October 30, 1995 | | 000 | A61K031/725 |
| WO 9530423 A3 | December 21, 1995 | | 000 | A61K031/725 |
| EP 760667 A1 | March 12, 1997 | E | 000 | A61K031/725 |
| HU 75868 T | May 28, 1997 | | 000 | A61K031/725 |
| CZ 9603089 A3 | January 14, 1998 | | 000 | A61K031/725 |
| JP 09512797 W | December 22, 1997 | | 265 | A61K031/725 |
| KR 97702728 A | June 10, 1997 | | 000 | A61K031/725 |
| SK 9601379 A3 | August 5, 1998 | | 000 | A61K031/725 |
| AU 696373 B | September 10, 1998 | | 000 | A61K031/725 |
| CA 2122519 C | February 20, 2001 | E | 000 | A61K031/725 |
| RU 2162327 C2 | January 27, 2001 | | 000 | A61K031/728 |

DESIGNATED-STATES: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE
KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TT UA
UG US UZ VN AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG AT BE
CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE

CITED-DOCUMENTS: CA 2097892; WO 9104058 ; WO 9316732 ; WO 9316733

APPLICATION-DATA:

| PUB-NO | APPL-DATE | APPL-NO | DESCRIPTOR |
|--------------|------------------|----------------|----------------|
| WO 9530423A2 | April 28, 1995 | 1995WO-CA00259 | |
| CN 1151118A | April 28, 1995 | 1995CN-0193689 | |
| AU 9524023A | April 28, 1995 | 1995AU-0024023 | |
| AU 9524023A | | WO 9530423 | Based on |
| CA 2122519A | April 29, 1994 | 1994CA-2122519 | |
| WO 9530423A3 | April 28, 1995 | 1995WO-CA00259 | |
| EP 760667A1 | April 28, 1995 | 1995EP-0917846 | |
| EP 760667A1 | April 28, 1995 | 1995WO-CA00259 | |
| EP 760667A1 | | WO 9530423 | Based on |
| HU 75868T | April 28, 1995 | 1995WO-CA00259 | |
| HU 75868T | April 28, 1995 | 1996HU-0002965 | |
| HU 75868T | | WO 9530423 | Based on |
| CZ 9603089A3 | April 28, 1995 | 1995WO-CA00259 | |
| CZ 9603089A3 | April 28, 1995 | 1996CZ-0003089 | |
| CZ 9603089A3 | | WO 9530423 | Based on |
| JP 09512797W | April 28, 1995 | 1995JP-0528564 | |
| JP 09512797W | April 28, 1995 | 1995WO-CA00259 | |
| JP 09512797W | | WO 9530423 | Based on |
| KR 97702728A | April 28, 1995 | 1995WO-CA00259 | |
| KR 97702728A | October 29, 1996 | 1996KR-0706101 | |
| KR 97702728A | | WO 9530423 | Based on |
| SK 9601379A3 | April 28, 1995 | 1995WO-CA00259 | |
| SK 9601379A3 | April 28, 1995 | 1996SK-0001379 | |
| AU 696373B | April 28, 1995 | 1995AU-0024023 | |
| AU 696373B | | AU 9524023 | Previous Publ. |
| AU 696373B | | WO 9530423 | Based on |
| CA 2122519C | April 29, 1994 | 1994CA-2122519 | |
| RU 2162327C2 | April 28, 1995 | 1995WO-CA00259 | |
| RU 2162327C2 | April 28, 1995 | 1996RU-0122884 | |
| RU 2162327C2 | | WO 9530423 | Based on |

INT-CL (IPC): A61 K 9/08; A61 K 31/19; A61 K 31/375; A61 K 31/495; A61 K 31/70; A61 K 31/725; A61 K 31/728; A61 K 45/06 ; A61 P 35/04

ABSTRACTED-PUB-NO: WO 9530423A

BASIC-ABSTRACT:

Use of effective dosage amts. ((A) and (B)) of pharmaceutical compsns. for (a) treatment of cancer in patients, (b) prevention of metastases in patients suffering from cancer, and (c) delivery of drugs to the lymph system and/or liver is new. Dosage amt. (A) comprises an anticancer drug and/or a drug suitable for use in treatment of cancer. It also comprises hyaluronic acid and/or a salt of this, with a mol. wt. < 750000 Daltons. The components are in sterile water suitable for injection. Dosage amt. (B) comprises (i) hyaluronic acid and/or a salt of this, with a mol. wt. < 750000 Daltons, (ii) a drug selected from non-steroidal antiinflammatory drugs and/or chemotherapeutic agents and opt. (iii) an antioxidant.

USE - The dosage form combination is esp. useful for treatment of breast cancer and prevention of metastases in patients with breast cancer.

ADVANTAGE - The combination reduces the risk of recurrence of the disease.

CHOSEN-DRAWING: Dwg.0/0

TITLE-TERMS: TREAT CANCER REDUCE CANCER METASTASIS ADMINISTER DOSE FORM CONTAIN
SODIUM HYALURONATE MOLECULAR WEIGHT BELOW DALTONS

DERWENT-CLASS: B05

CPI-CODES: B04-C02E; B04-C02F; B14-H01B;

CHEMICAL-CODES:

Chemical Indexing M2 *01*

Fragmentation Code

A111 A960 C710 F012 F013 F014 F015 F113 H4 H403
H421 H482 H8 J5 J522 K0 L8 L818 L821 L832
L9 L942 L960 M280 M312 M321 M332 M343 M373 M391
M411 M431 M510 M521 M530 M540 M630 M782 M903 M904
M910 P633

Specific Compounds

08147M

Registry Numbers

0035U

Chemical Indexing M1 *02*

Fragmentation Code

J0 J011 J1 J111 J3 J321 K0 L8 L814 L832
L834 M210 M211 M262 M280 M281 M320 M423 M431 M630
M782 M903 M904 P633 V735

Specific Compounds

07175M

Chemical Indexing M1 *03*

Fragmentation Code

J0 J011 J1 J111 J3 J321 K0 L8 L814 L832
L834 M210 M211 M262 M280 M281 M320 M423 M431 M630
M640 M650 M782 M903 M904 P633 V735

Specific Compounds

06437M

Chemical Indexing M1 *04*

Fragmentation Code

J0 J011 J1 J111 J3 J321 K0 L8 L814 L832
L834 M210 M211 M262 M280 M281 M320 M423 M431 M782
M903 M904 P633 V735

Specific Compounds

03231M

UNLINKED-DERWENT-REGISTRY-NUMBERS: 0035U

SECONDARY-ACC-NO:

CPI Secondary Accession Numbers: C1996-003250